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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,582	07/25/2003	Peter B. Vander Horn	020130-001510US	3008

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,582	VANDER HORN ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *11-24,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-10,25 and 27-30* is/are rejected.

7)☒ Claim(s) *7 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment of the specification and of claims 1-6, in the paper of 1/31/2007, is acknowledged. Claims 1-32 are still at issue and are present for examination.

Applicants' arguments filed on 1/31/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Election/Restrictions

Applicant's continued argument of the previous restriction requirement is acknowledged and continues to be carefully considered and continues to be found nonpersuasive on the basis that the restriction as previously stated is proper for the reasons previously stated. With respect to applicants arguments that claim 1 is a genus claim that if restricted would preclude applicants from the full scope of applicants invention, applicants argument is not persuasive. Just because claim 1 is generic to another claim does not make it a "genus type" claim. Further as previously stated, the proper restriction of this claim would still allow applicants to claim the full scope of applicant's invention, as this claim would still be fully considered on its merits. Such a claim could properly be divided into multiple claims, such that an undue burden is not presented, and would result in a increase in the quality of examination of applicants claimed subject matter.

The requirement is still deemed proper and continues to be made FINAL.

Claims 11-24, 31 and 32 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure is objected to because of the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth: The following portions of the specification list sequences which appear to meet the definition for an amino acid sequence, but do not have an associated SEQ ID No: Figures 5 and 6 or the description of these figures.

Applicant's amendment of the description of the figures is acknowledged. It is requested that applicants additionally amend the description of the figures to specify which sequences are associated with which sequence identifiers.

Appropriate correction is required.

Claim Objections

Claims 7 and 26 are objected to because of the following informalities:

Claims 7 and 26 each depend from rejected claims.

Claims 7 and 26 contain non-elected subject matter.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8, 9, 10, 25 and 27-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a hybrid polymerase comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any hybrid polymerase comprising SEQ ID NO: 23 and having a mere 85% identity over 700 contiguous amino acids to SEQ ID NO: 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1-6, 8, 9, 10, 25 and 27-30. In response to this rejection applicants have amended claims 1-6 and argue the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that applicants provide guidance as to which residues can be substituted in the claimed polymerase sequences and that the hybrid polymerases exemplified in the specification demonstrate that more than one substation can readily occur in a parental polymerase, i.e. SEQ ID NO: 24. Applicants further submit based upon the examples detailed in the specification, the guidance provided by applicants for selecting residues for substitution, and the level of knowledge

in this advanced art that one of skill would be able to identify members of the claimed genus of polymerase proteins without undue experimentation.

With respect to guidance, applicants submit that the application provides guidance as to sites within the polymerase protein reference sequence that tolerate substitutions, as applicants submit that the genus of claimed proteins is derived from two parental polymerases, Pfu and Deep Vent ®. Applicants further submit that a member of the claimed genus of proteins must (i) have a specified identity to Pfu polymerase, (ii)comprise SEQ UID NO: 23 and (iii) comprise at least one substituted residue at a site conserved between Pfu and Deep Vent ®.

Applicants submit that in addition to the above discussed guidance, applicants have taught specific examples of active polymerase proteins that have been obtained by following the teachings of the specification. For example, applicants submit that they teach at least six hybrid polymerase proteins that were isolated from libraries constructed to provide hybrid polymerases having the characteristics set forth in claim 1.

Applicants further submit that the prior art provides detailed structural and functional analyses of polymerase B proteins, for example, Hopfner et al. Proc. Natl. Acad. Sci. USA 96:2600-2605 provides a crystal structure of an Archael DNA polymerase and that Hopfner et al. teaches that the structure of the Thermococcus gorgonarius (Tgo) polymerase allows the generation of a structure based sequence alignment of the archael subfamily of type B DNA polymerases, including Pfu polymerase.

Finally, applicants submit that the specification teaches one of skill in the art how to practice the claimed invention.

Applicant's complete argument is acknowledged and has been carefully considered, however continues to be found nonpersuasive for the reasons previously presented and reiterated herein.

As previously stated, the claims are so broad as to encompass any hybrid polymerase comprising SEQ ID NO: 23, a mere twenty five amino acid polypeptide and having a mere 85% identity to SEQ ID NO: 24, with the additional limitation that the polymerase polypeptide must have at least one substitution at a position designated "X" in SEQ ID NO: 26. It is noted that the encompassed mutations are not limited to those positions designated "X" in SEQ ID NO: 26.

With respect to applicants provided guidance, while applicants have designated a fraction of those potential residues which may be mutated as well as the amino acid to which these mutations may be changed, applicants have not given guidance beyond these small fraction of potential mutations. Similarly the examples presented in applicant's specification provide but a small fraction of the encompassed mutant "hybrid polymerases" encompassed by applicants claimed genus. While the level of skill in the art may be high, the guidance which is needed to sufficiently enable the scope of the claimed genus of hybrid polymerase proteins is insufficient.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a hybrid polymerase) requires that one

of ordinary skill in the art know or be provided with sufficient guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities, even within the scope of the claimed hybrid polymerase proteins having 85% sequence identity to SEQ ID NO: 24. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. While applicants have provided some guidance as to some residues which may be substituted and the amino acids which they may be substituted with, as well as the crystal structure information of a similar polymerase protein, such is not sufficient to enable the scope of the genus of claimed hybrid DNA polymerases.

As previously stated the specification does not sufficiently establish:: (A) regions of the protein structure which may be modified without effecting hybrid polymerase activity; (B) the general tolerance of the specified hybrid polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the polymerase activity claimed and the fact

that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having the claimed polymerase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any hybrid polymerase comprising SEQ ID NO: 23 and having a mere 85% identity to SEQ ID NO: 24. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those hybrid polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

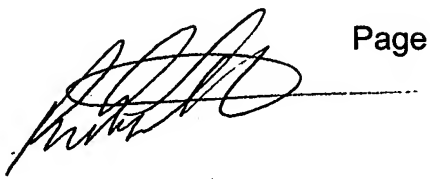
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
4/23/2007